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## Modern Management of Cornual Ectopic Pregnancy

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### 1. Introduction

Cornual ectopic or interstitial ectopic is a pregnancy that implants in the intrauterine portion of fallopian tube. Due to its location, there is an inherent difficulty in the diagnosis and treatment leading to high mortality compared with other ectopic pregnancies.

Transvaginal Ultrasound scan is the most useful diagnostic tool for establishing the diagnosis though serial  $\beta$ -HCG and even laparoscopy are sometimes needed to confirm the diagnosis.

Due to the high risk of rupture with serious or fatal bleeding, there is no role for the expectant management. Surgery is the most common management option. Though traditionally laparotomy is the main surgical intervention, recently increasing number of laparoscopic or even hysteroscopic approach have been used. Injection of Methotrexate locally or systemically has also been used successfully.

### 2. Anatomy

Each Fallopian tube is usually 10 cm long with variations in length from 7 to 14 cm. The abdominal ostium is situated at the base of a funnel-shaped expansion of the tube, the infundibulum. Medially, it opens into the thin-walled ampulla forming more than half the length of the tube and 1 or 2 cm in outer diameter; it is succeeded by the isthmus, a round and cord-like structure constituting the medial one-third of the tube and 0.5-1 cm in outer diameter. The isthmus continues through the uterine wall to the uterine cavity forming the interstitial or cornual portion of the tube. This segment of the tube is about 1 cm in length and 1 mm in diameter. (Diamond, 1988)

### 3. Epidemiology

Interstitial (cornual) pregnancy is a rare type of ectopic pregnancy, accounting for 2-4% of all tubal pregnancies (Lau S & Tulandi T, 1999). The surrounding myometrial tissue allows progression of the pregnancy into the second trimester but rupture at such an advanced gestation may result in catastrophic haemorrhage with a mortality rate of up to 2%. This high mortality rate is partially due to the difficult challenging diagnosis as well as the speed of haemorrhage. (Tulandi T & Al-Jaroudi D, 2004; Vicino M et al, 2000; Dilbaz S et al, 2005; Rock J et al, 2003)

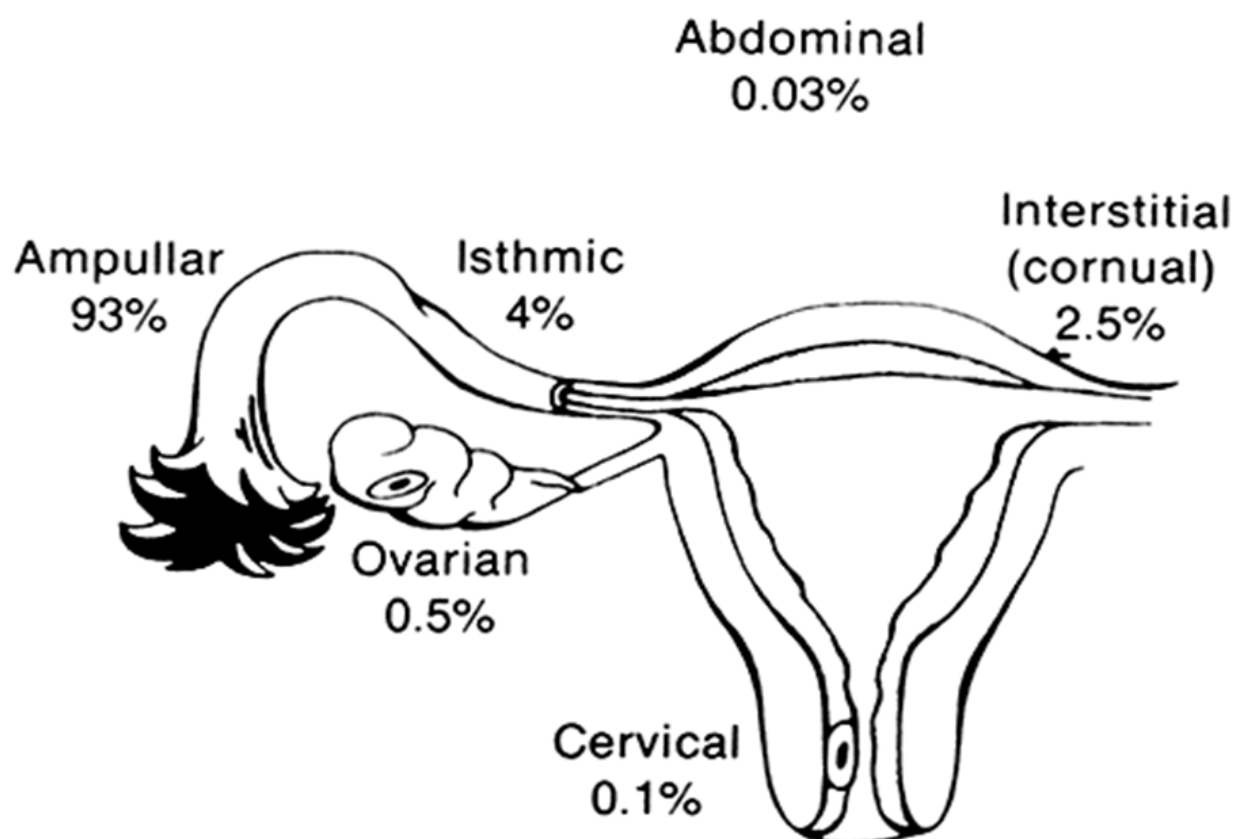


Fig. 1. Sites and frequencies of ectopic pregnancy.

#### 4. Risk factors

Cornual ectopics share the common risk factors of other ectopic pregnancies which are:

##### 4.1 Pelvic inflammatory disease (PID)

The incidence of tubal damage after the first episode of PID is 13%. This incidence increases to 35% after the second episode of PID and to 75% after the third episode. A history of salpingitis increases the risk of ectopic pregnancy by 4 fold. (Westrom L et al, 1981)

##### 4.2 History of previous ectopic pregnancy

After one ectopic pregnancy, patients have a 7-13 fold increase in the likelihood of another ectopic pregnancy. Method of management of previous ectopic pregnancy influences the chance of recurrence. The incidence is increased according to the size of the ectopic pregnancy specially if treated salpingostomy. The incidence of recurrence of ectopic is 18% and 8% after treatment with salpingostomy and salpingectomy respectively though the chance of future intrauterine pregnancy is 89% after salpingostomy compared with 66% after salpingectomy. (Silva Pet al, 1993)

##### 4.3 History of tubal surgery and conception after tubal ligation

Salpingectomy, salpingostomy, neosalpingostomy, fimbrioplasty, tubal reanastomosis, and lysis of peritubal or periovarian adhesions are associated with an increased risk of ectopic pregnancies.

One third of patients who conceive after a tubal ligation are reported to experience an ectopic pregnancy. Ectopic pregnancies following tubal ligation usually occur 2 or more years after sterilization, rather than immediately after. In the first year, only about 6% of sterilization failures result in ectopic pregnancy. (DeStefano F, 1982)

#### **4.4 Assisted reproductive technology**

The risk of ectopic pregnancy increases if the patient has conceived following an assisted reproductive technique, such as in vitro fertilization (IVF) or gamete intrafallopian transfer (GIFT). The ectopic pregnancy rate quoted as 1.6% and the heterotopic pregnancy rate as 13%.

#### **4.5 Use of an intrauterine contraceptive device (IUD)**

Conception with an IUD in place is coupled with 3-4% risk of ectopic pregnancy which again more than double the background risk. This is more prominent as IUD decreases the intrauterine conception rate. (Ory HW, 1981)

#### **4.6 Increasing age**

Women over 40 years of age have a 3 – 4 fold increase in the risk for developing an ectopic pregnancy compared to women aged 15-24 years. This has been attributed to a possible progressive loss of myoelectrical activity along the fallopian tube with ageing or to the deterioration in the quality of the fertilised egg.

#### **4.7 Smoking**

Smoking has been shown to increase the risk of ectopic pregnancy by 3 fold. To date, no study has supported a specific mechanism by which cigarette smoking affects the incidence of ectopic pregnancy however, delayed ovulation, altered tubal motility, or altered immunity have been suggested. (Coste J et al, 1991)

#### **4.8 Previous pelvic surgeries**

Previous pelvic surgeries have shown to increase the risk of ectopic pregnancy. Right ectopic pregnancy seems to be more frequent than left due to history of appendicitis or even subclinical subacute inflammation of the appendix.

#### **4.9 Other**

Salpingitis isthmica nodosum like any other inflammation of the tubes has been thought to be associated with increase incidence of ectopic pregnancy.

### **5. Presentation**

The wide spread of specialised early pregnancy units and the abundance of ultrasound facilities led to early diagnosis of cornual ectopics. There is an increasing incidence of asymptomatic ectopics compared with more traditional presentation of lower abdominal pains and vaginal bleeding.

Ruptured ectopics can however present with typical signs of haemorrhagic shock, which include pallor, tachycardia, hypotension and oliguria. The assessment of the uterine size is rarely helpful and cervical excitation is not a specific sign in cornual ectopic.

## 6. Diagnosis

### 6.1 Ultrasound

Trans vaginal ultrasound scan is the corner stone for the early diagnosis of cornual ectopic. The ultrasonographic diagnosis of cornual ectopic is challenging and needs expert hands. The eccentric position of the gestational sac with an empty uterine cavity and the presence of a thin (less than 5 mm) or even absent myometrium surrounding the sac are highly suggestive of cornual ectopic pregnancy. (Timor-Tritsch IE et al, 1992; Johnson PT& Shah C). The diagnosis may be helped with the use of Doppler studies showing increase vasculature around the gestational sac. (Abraham D& Silkowski C, 2010). This is sometimes described as a ring of vessels (Ring of fire). It also helps to exclude pseudosac due to endometrial reaction. The gestational sac is usually seen away from the thickened endometrium associated with the pregnancy.

The ultrasound picture of cornual ectopic can be very similar to that of an early pregnancy in a bicornuate uterus or a fibroid uterus. Therefore the diagnosis of cornual ectopic should be made with caution, keeping in mind the possible differential diagnosis. (Abraham D& Silkowski C, 2010).

In experienced hands, trans-vaginal ultrasound can establish diagnosis of cornual ectopics in nearly 71% of cases. (Tulandi T& Al-Jaroudi D, 2004).

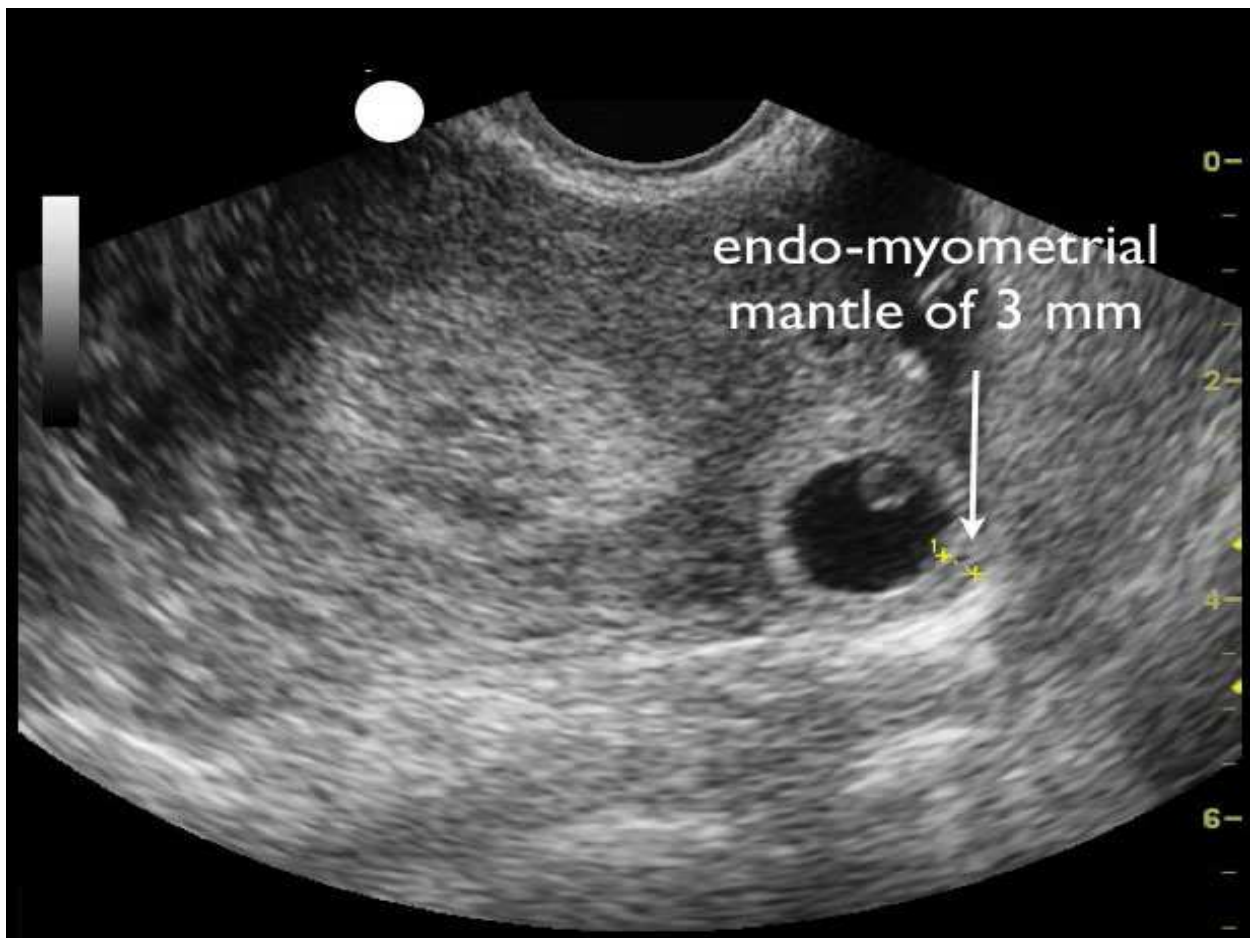


Fig. 2. Cornual ectopic located eccentrically within uterine cavity. Note the thin layer of myometrial tissue on the lateral aspect of gestational sac.





Fig. 3. Bicornuate uterus mimicking cornual ectopic pregnancy. Transverse transabdominal view shows bicornuate uterus with a pregnancy in right horn

The use of 3-D and 4-D improves sensitivity of establishing the diagnosis especially when contrast is used. (Lee GS et al, 2005; Chou MM et al, 2005). However, lack of its availability in many units limits their use as the recommended methods.

### 6.2 Serial $\beta$ hCG

Ectopic pregnancy is known to be associated with a suboptimal increase or plateau of serum  $\beta$  hCG. (Banerjee S et al, 1999; Hajenius P et al, 1995) With a detection rate of 97% and a specificity of 77%, serial serum  $\beta$  hCG is useful to establish the diagnosis of ectopic pregnancy in association of the sonographic findings. (Cacciatore B et al, 1990)

In cornual ectopics, there are reports of doubling of serum  $\beta$  hCG, therefore the value of performing serial serum  $\beta$  hCG is doubtful and the results should be interpreted with caution. (Abraham D & Silkowski C, 2010)

### 6.3 Role of laparoscopy

Laparoscopy is an essential diagnostic tool as well as a possible treatment method route for suspected cornual ectopics. However, in cornual ectopics, difficulty arises with small ectopic masses that can be missed.

Experienced laparoscopic operator is crucial in such cases in order to have the ability to deal with possible high risk of heavy bleeding when treatment of cornual ectopics is accomplished laparoscopically.

## 7. Management of cornual ectopic

Early diagnosis allows a varied choice of treatment options with a high possibility of preserving fertility.



Fig. 4. Left cornual ectopic

## 7.1 Medical treatment

### 7.1.1 Systemic methotrexate

An increasing number of cornual ectopic have been treated with Methotrexate. This is mainly due to the accuracy of the ultrasound scan in confirming the diagnosis as well as the wide spread experience in the use of Methotrexate in the management of ectopic pregnancies.

Patients suitable for medical management should have minimal or no symptoms, be haemodynamically stable (Royal College of Obstetricians and Gynaecologists, 2004) , and with  $\beta$  hCG < 3000 IU. (Yao M& Tulandi T, 1997; Sowter M& Frappell J, 2002; Kelly H et al, 2006; Teal SB, 2006). It is more successful if no fetal heart beats(Yao M& Tulandi T, 1997; Sowter M& Frappell J, 2002) are detected in the ectopic pregnancy and the ectopic size is < 4 cm. Patients should be willing to attend regular follow up and have no contraindication for Methotrexate. (Royal College of Obstetricians and Gynaecologists, 2004)

There is no clear data regarding the effect of ectopic size on the treatment outcome but the larger the ectopic the more likely the treatment fails. (Lipscomb G et al, 1999)The patient should be given clear and written information about the Methotrexate treatment protocol, its success rate and the possible adverse effects. (Royal College of Obstetricians and Gynaecologists, 2004) A clear follow-up protocol should be explained to the women with explanation of possible symptoms or ruptured ectopic. (Royal College of Obstetricians and Gynaecologists, 2004) The possible need for further treatment either electively or as an in case of emergency should be documented and the women should be given a contact number for advice or emergency. (Royal College of Obstetricians and Gynaecologists, 2004)

Identified patients for medical treatment should have blood tests for Full Blood Count, Liver Function Tests and Renal function tests before starting the Methotrexate treatment. (Royal College of Obstetricians and Gynaecologists, 2004; Kelly H et al, 2006; Teal SB, 2006).

The Body surface area is calculated and a single dose 50 mg/m<sup>2</sup> is given Intra-muscularly. This dose has been shown to be effective with < 15% needs additional treatment with least side effects compared to other regimens. (Royal College of Obstetricians and Gynaecologists, 2004; Yao M& Tulandi T, 1997; Sowter M& Frappell J, 2002; Kelly H et al, 2006; Teal SB, 2006) The possible side effects of Methotrexate includes, GIT upset, Conjunctivitis and photosensitivity, pneumonitis, reversible alopecia, liver or renal impairment, myelosuppression and possible teratogenicity, so the patient should not conceive within 3 months of completion of treatment. (Royal College of Obstetricians and Gynaecologists, 2004; Barnhart KT et al, 2003).

Following the injection of Methotrexate, follow-up  $\beta$  hCG should be done on day 4 and day 7 after the treatment aiming check to for the decreasing levels. An initial rise may be observed but an expected drop of > 15% is expected between day 4 and day 7 in successfully treated ectopics. (Yao M& Tulandi T, 1997; Sowter M& Frappell J, 2002) A weekly follow-up is needed till non pregnant levels of  $\beta$  hCG. (Royal College of Obstetricians and Gynaecologists, 2004)

Liver function tests may need to be repeated at the same time as the  $\beta$  hCG due to the possible side effects of Methotrexate on Liver Function. Throughout the follow-up duration, the patients should maintain an easy access to the hospital and informed to come back if they experience pain or bleeding. (Sowter M et al, 2001; Mol B et al, 1999)

The systemic route of administration offers advantages over local injection of the ectopic gestation as it is less invasive and not operator dependent. (Royal College of Obstetricians and Gynaecologists, 2004)

### 7.1.2 Local methotrexate

Methotrexate can be injected directly into the ectopic sac through the myometrium under transvaginal ultrasound guidance or alternatively during the laparoscopic procedure. (Timor-Tritsch IE, 1997; Benifla JL et al, 1996; Onderoglu LS et al, 2006)

Either of these treatment options aimed to reduce the systemic exposure and side effects of Methotrexate with a chance of spontaneous resolution of ectopics in some studies can be as high as 100%. (Monteagudo A et al, 2005)

Local potassium chloride injection has been used as alternative to Local Methotrexate with promising results. It is used mainly if the patient is keen on conceiving soon after the ectopic. (Doubilet PM et al, 2004)

## 7.2 Surgical management

### 7.2.1 Surgical techniques

Surgical management depends mainly on the presenting condition of the patient and the skills of the operating surgeon. Cornual ectopic has been reported to be treated by variation of procedures mainly cornuotomy, cornual resection and a more radically a hysterectomy. The latter has only a role in a life saving condition when other methods has been tried and exhausted. However, in experienced hand, it is nearly always possible to avoid a hysterectomy even in haemodynamically unstable patients with ruptured ectopic pregnancy.

In cornuotomy or cornual resection, the usage of diathermy or harmonic scalpel in the dissection can help in the reduction of blood loss. Intracorporeal knots of the PDS or Vicryl stitches can be used to close the cornual resection site. The round ligament could be used to



cover the cornual resection site aiming to reduce post operative adhesions and to facilitate the closure of resection site especially when large size ectopics are removed. (Api M& Api O, 2010; MacRae R et al, 2009; Tinelli A et al, 2010; Moon HS et al, 2000).

No clear data is available to compare risks of subsequent ectopic and the chances of persistent trophoblastic disease after cornual resection versus cornuotomy. Preservation of fertility following these surgical techniques has been confirmed. However, there is an expected reduction in chances of conception due to loss of the function of that tube. Future pregnancy is usually ending by a caesarean section due to the risk of uterine rupture. (Lindheim SR et al, 2006)

Uterine artery ligation may help to conserve the uterus in ruptured cornual ectopic as it can aid the homeostasis if conservative surgery attempted via open approach (Khawaja N et al, 2005).

### 7.2.2 Open approach versus laparoscopic approach

Laparotomy is preferred in hemodynamically unstable patients with signs and symptoms of hypovolaemic shock. Senior operator is necessary in such situation where the bleeding might be severe and life threatening because of the enormous blood supply to the uterine cornua especially when the gestation is advanced at time of ectopic rupture. (Grimbizis GF et al, 2004)

Laparoscopic approach is preferred over the laparotomy for unruptured cases provided a skilled laparoscopic surgeon is available. (Hill GA et al, 1989; Grobman WA& MP Milad, 1998) Laparoscopic approach is associated with less intra-operative bleeding, less post operative pain and analgesia requirement, shorter hospital stay and fewer post operative adhesions. (Royal College of Obstetricians and Gynaecologists, 2004)

No clear data available to compare chances of having a subsequent intrauterine pregnancy between the open versus the laparoscopic approaches for cornual ectopics however the latter is thought to be possibly associated with less risk of recurrent ectopics.

### 7.2.3 Vaginal approach

In the last decade, trans-cervical approach for the treatment of cornual ectopic has been advocated. The cornual ectopic is disturbed under hysteroscopic, laparoscopic or even ultrasound guidance. (Thakur Y et al, 2004)

It avoids extensive surgery and can be useful for women who are reluctant to undergo medical treatment with Methotrexate or in whom this treatment failed. (Pal B et al, 2003)

The approach involves identification and disturbance of ectopic sac through a vaginal approach using a curette. The products of conception then removed using polyp forceps or a suction curette. (Minelli L et al, 2003; Meyer WR& Mitchell DE, 1989; Sanz LE& Verosko J, 2002) The use of laparoscopic or ultrasonic guidance is recommended due to the high risk of perforation. (Marian Morgan et al, 2009) Also this approach is not aimed at evacuation of all the product of conception as this could be associated with perforation. It is only aiming at disturbing the pregnancy and removing some of the product safely. (Marian Morgan et al, 2009) Therefore, follow-up is essential to ensure complete resolution of the pregnancy. In severe bleeding, laparoscopic local injection of vasopressin may reduce intraoperative bleeding. (Pal B et al, 2003)

This approach is simple and associated with less morbidity than abdominal approach. It is associated with less bleeding as the myometrium remained undisturbed, rapid recovery and a shorter post-operative stay resulting in financial and psychological benefits.

It is also possible that it would have less effect on fertility than abdominal approach and further intrauterine pregnancies could be managed as low risk with no increase chance of uterine rupture and hence normal vaginal delivery could be the choice of the mode of delivery.

#### 7.2.4 Serum $\beta$ hCG clearance

Serial serum  $\beta$  hCG should be measured after any conservative surgical treatment of corneal ectopic to ensure complete resolution. The duration of the monitoring is of little significant but a declining titre is essential and needs monitoring at intervals till resolution. (Kamrava MM et al, 1983)

#### 7.3 Expectant management

Cornual ectopics are associated with high risk of rupture that could occur as late as 10 – 16 weeks. . (Abraham D& Silkowski C, 2010). Rupture of a corneal ectopic at that late gestation can cause profuse intraperitoneal bleeding which can be life threatening. The Confidential Enquiry into Maternal and Child Health (CEMACH) report for 2000–02 confirmed that 4 out of 11 deaths due to ectopic pregnancies (36%) were corneal ectopics. (Confidential Enquiry into Maternal and Child Health, 2004)

Therefore, expectant management has no place in confirmed cornual ectopic. (Kok-Min S et al, 2004)

### 8. Effect of cornual ectopic treatment on future fertility

With regard future fertility, cornual ectopic is associated with higher risk of recurrent ectopic compared with other types of ectopic pregnancy. If the uterus is conserved, there is an increased incidence of uterine rupture at the surgical site in future pregnancies in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters especially in the cases where the sac excision leads to defective myometrium &/or the uterine cavity has been opened. However, the data about the absolute increase in such risk is still conflicting. (Lau S& Tulandi T, 1999; Weissman A& Fishman A, 1992)

There is a view about reinforcing the uterine wall with the use of round ligament especially if the cavity is opened. Again, no evidence yet has shown a proven benefit of such techniques. (Chatterjee J et al, 2009)

With regard the mood of delivery in subsequent pregnancy, caesarean section is recommended by many clinicians however, no evidence yet available to evaluate the safety of caesarean section versus vaginal delivery after cornual ectopic treatment. (Downey GP& Tuck S, 1994)

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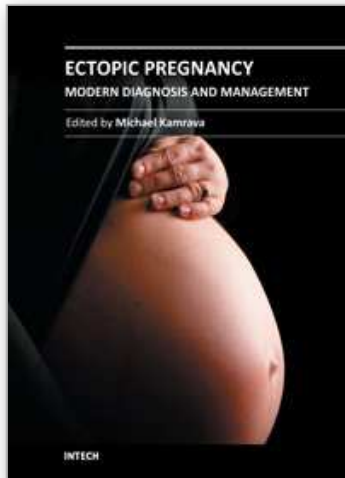
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## **Ectopic Pregnancy - Modern Diagnosis and Management**

Edited by Dr. Michael Kamrava

ISBN 978-953-307-648-5

Hard cover, 248 pages

**Publisher** InTech

**Published online** 26, October, 2011

**Published in print edition** October, 2011

Ectopic pregnancy is the second major cause of maternal mortality in the United States and a leading cause of maternal morbidity and mortality in the world. This book contains the practical methods to early diagnosis of various forms of ectopic pregnancies and their modern management. Ectopic Pregnancy - Modern Diagnosis and Management is a comprehensive book which guides the reader through all features of ectopic pregnancy, both practical and academic, covering all aspects of diagnosis and management of ectopic pregnancy in a clear, concise, and practical fashion. The book is organized so that it can either be read cover to cover for a comprehensive tutorial or be kept desk side as a reference to the ectopic pregnancies. Each chapter introduces a number of related ectopic pregnancy and its diagnosis, treatment and co-morbidities supported by examples. Included chapters bring together valuable materials in the form of extended clinical knowledge from practice to clinic features.

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Maged Shendy and Rami Atalla (2011). Modern Management of Cornual Ectopic Pregnancy, Ectopic Pregnancy - Modern Diagnosis and Management, Dr. Michael Kamrava (Ed.), ISBN: 978-953-307-648-5, InTech, Available from: <http://www.intechopen.com/books/ectopic-pregnancy-modern-diagnosis-and-management/modern-management-of-cornual-ectopic-pregnancy>

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